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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/575,530 | 01/04/2007 | Francoise Jeanne Gellibert | PB60226USW | 3651 |

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GLAXOSMITHKLINE
CORPORATE INTELLECTUAL PROPERTY, MAI B482
FIVE MOORE DR., PO BOX 13398
RESEARCH TRIANGLE PARK, NC 27709-3398

| EXAMINER |
|---|
| CHUNG, SUSANNAH LEE |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1626 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 06/04/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USCIPRTP@GSK.COM
LAURA.M.MCCULLEN@GSK.COM
JULIE.D.MCFALLS@GSK.COM

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/575,530 | GELLIBERT ET AL. | |
| | Examiner | Art Unit | |
| | SUSANNAH CHUNG | 1626 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,4,7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1, 4, 7 and 8 are pending in the instant application. Claims 2-3 and 5-6 are canceled by preliminary amendment.

### *Priority*

This application is a 371 of PCT/EP04/11386, filed 10/07/2004.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) by application no. 0323702.1 filed in the United Kingdom Patent Office on 10/09/2003, which papers have been placed of record in the file. The application names an inventor or inventors named in the prior application.

### *Information Disclosure Statement*

The information disclosure statement (IDS), filed on 04/10/2006 has been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

### *Claim Rejections - 35 USC § 112, 1st paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims, for the reasons describe below.

As stated in MPEP 2164.01(a), "there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a

disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

The factors to be considered when determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, were described in In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) as:

1. the nature of the invention;
2. the breadth of the claims;
3. the state of the prior art;
4. the relative skill of those in the art;
5. the predictability or unpredictability of the art;
6. the amount of direction or guidance presented [by the inventor];
7. the presence or absence of working examples; and
8. the quantity of experimentation necessary [to make and/or use the invention].

The eight Wands factors are applied to Claims 7 and 8 of the present invention below:

*(1) The Nature of the Invention*

A method of treating an hPPAR mediated disease or condition in general or wherein the mediated disease or condition is dyslipidemia, syndrome X, heart failure, hypercholesteremia, cardiovascular disease, type II diabetes mellitus, type I diabetes, insulin resistance, hyperlipidemia, obesity, anorexia bulimia or anorexia nervosa.

*(2) The Breadth of the claims*

Claims 7 and 8 will be give its broadest reasonable interpretation. The applicable rule for interpreting the claims is that "each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." See MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). In view of this rule, Claim 7 which is directed to treating all hPPAR mediated diseases or conditions in general will be interpreted to encompass all types of diseases or conditions associated with hPPAR. Claim 8 which is directed to a specific list of disorders (i.e. dyslipidemia, syndrome X, heart failure, hypercholesteremia, cardiovascular disease, type II diabetes mellitus, type I diabetes, insulin resistance, hyperlipidemia, obesity, anorexia bulimia or anorexia nervosa) will be interpreted to encompass those disorders only.

*(3) The state of the prior art*

The state of the pharmaceutical art in general involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat or prevent diseases related to hPPAR).

The state of the art at the time of this application is that the etiology and treatment of all diseases or conditions associated with hPPAR is not well understood. Treatment of hPPAR related disorders and conditions is challenging and highly unpredictable. Adding to the challenge are the many different diseases that could be encompassed by hPPAR and all the different mechanisms of action and no two types of hPPAR related disease could be said to share the same method of treatment.

Currently, three mammalian Peroxisome Proliferator-Activated Receptors have been isolated and termed PPAR-alpha, PPARgamma, and PPAR-delta (also known as NUC1 or PPAR-beta). These PPARs regulate expression of target genes by binding to DNA sequence elements, termed PPAR response elements (PPRE). To date, PPRE's have been identified in the enhancers of a number of genes encoding proteins that regulate lipid metabolism suggesting that PPARs play a pivotal role in the adipogenic signaling cascade and lipid homeostasis.

The use of PPAR agonists to treat dyslipidemia has been known for several decades because of their triglyceride lowering an dhigh density lipoprotein cholesterol elevating effects. The use of PPAR agonists to treat cardiovascular disorders is being researched and has a promising future, but it is unclear whether they will indeed be used in treating cardiovascular disorders until more research is done. Pharm. Res., Vol. 21(9), September 2004, pp. 1531-1538, especially p. 1536.

*(4) The relative skill of those in the art*

The level of skill in the art (pharmaceutical chemists, physicians) would be high.

*(5) The predictability or unpredictability of the art*

It is noted that the pharmaceutical art generally is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement varies inversely with the degree of unpredictability in the factors involved. In re Fisher, 427 F.2d 833, 839. Therefore, the more unpredictable an area, the more specific enablement is needed in order to satisfy the statute. Added to the

unpredictability of the art itself is the question whether use of PPAR agonists to treat disorders such as dyslipidemia could reliably and predictably applied to the treatment of all types of hPPAR disorders. There is no absolute predictability, even in view of the high level of skill in the art.

*(6) The amount of direction or guidance presented (by the inventor)*

The state of the art and specification in the present invention discloses that the instantly claimed compounds are PPAR agonists and could treat dyslipidemia. (See specification pages 2, 13 and 14 and van Raalte journal).

*(7) The presence or absence of working examples*

The specification shows the activity of the instantly claimed compound in one cell line, CV-1 cells. There is no IC50 data or population data or other data to support the use of the instantly claimed compound in any other cell line.

*(8) The quantity of experimentation necessary (to make and/or use the invention)*

Given the absence of direction or guidance (or working examples) in the specification for the role of the instantly claimed compounds in the treatment of all hPPAR related disorders, it would cause a skilled artisan an undue amount of experimentation to practice this invention to determine which patients with which diseases would benefit from which of the many claimed compounds within the scope of the invention with a reasonable expectation of success.

The instant breadth of the claim(s) is broader than the disclosure, specifically, the instant claim is directed to the treatment of hPPAR disorders in general, but the

specification, prior art or instant disclosure does not provide support for this. The state of the art is the PPAR agonists can treat dyslipidemia only.

***Obviousness Double Patenting***

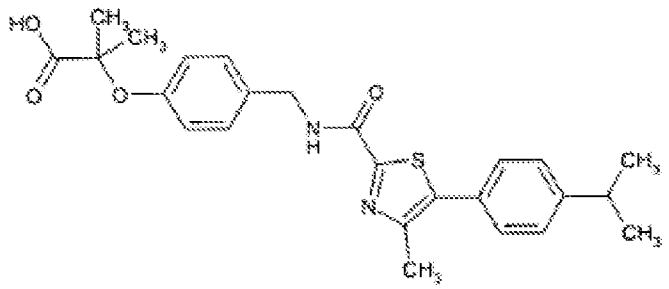
The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4, 7 and 8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-6 of US Pat No 7,157,479 (`479 Pat).

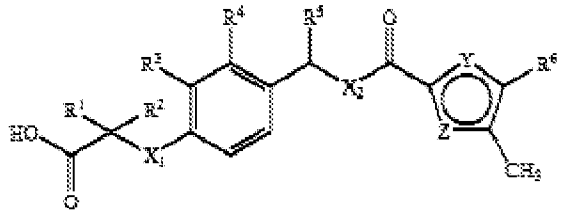
Instant claim 1 claims a compound of



(1)

formula .

The `479 Pat claims a compound of formula



and the species 2-methyl-2 [4-[[(4-methyl-5-[4-ethylphenyl]thiazol-2-ylcarbonyl) amino]methyl]phenoxy]propionic acid in claim 3. See `479 Pat, column 19, second compound.

The difference between the `479 Pat and the instant claims is that the instant claim substitutes methyl for hydrogen.

Although the conflicting claims are not identical, they are not patentably distinct from each other because one of ordinary skill in the art would recognize that substituting methyl for hydrogen is well known in the art. Hydrogen and methyl are deemed obvious variants. In re Wood, 199 USPQ 137

As such, the substitution of methyl for hydrogen is obvious and does not change the method of making of the claimed compounds or the method of using the compounds, i.e. the utility of the compounds in treating hPPAR disorders. The

motivation to optimize this class of thiazole compounds is the expectation that they will have similar pharmacological properties as hPPAR agonists.

In the absence of showing unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention when faced with the `479 Pat to make and use the instantly claimed compounds.

The instant obviousness rejection is based on the close structural similarity of the instantly claimed compounds to the prior filed application compounds and the common utility shared among the compounds. There is an expectation among those of ordinary skill in the art that similar structural compounds will have similar properties and that modification of a known structure is mere experimentation within the means of a skilled artisan. See MPEP 2144.09(I). Therefore, claims 1, 4 and 7-8 are rejected as obvious over the `479 Pat.

### *Objections*

Claim 1 is objected to because the claim states formula (I) and (1). It is unclear, which designation is intended. Appropriate correction is required.

### *Telephone Inquiry*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Chung whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Susannah Chung/
Examiner, Art Unit 1626